Clinical trial results:
A Prospective 3-Year Follow-up Study in Subjects Treated in a Preceding Phase 2 or 3 Study With a Regimen Containing Odalasvir and AL-335 With or Without Simeprevir for the Treatment of Hepatitis C Virus (HCV) Infection

Summary

EudraCT number	2016-002608-19
Trial protocol	BE DE PL ES
Global end of trial date	13 February 2018

Results information

Result version number	v1 (current)
This version publication date	01 March 2019
First version publication date	01 March 2019

Trial information

Trial identification

Sponsor protocol code	64294178HPC3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03099135
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg, 30, Beerse, Belgium, 2340
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to evaluate the durability of sustained virologic response (SVR) in subjects treated for hepatitis C virus (HCV) infection in a preceding Phase 2 or Phase 3 study who had achieved SVR at last post-therapy visit of the parent study (LPVPS).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. The safety assessments included monitoring of adverse events, clinical laboratory assessments (serum chemistry, hematology, coagulation, and alpha-fetoprotein), and electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	New Zealand: 43
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Singapore: 2
Worldwide total number of subjects	54
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	52
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 54 subjects were enrolled from parent studies AL-335-604 (NCT02569710) and 64294178HPC2001 (NCT02765490) and analyzed in this follow-up study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SVR at LPVPS

Arm description:

Subjects who completed the last post-therapy visit of the parent study (LPVPS) (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of hepatitis C virus (HCV) infection, and who agreed to participate in this follow-up study was assessed for durability of sustained virologic response (SVR), incidence of late viral relapse, presence and long term-persistence of resistance associated substitutions (RAS) and liver disease status. SVR at the LPVPS is defined as subjects who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study, and maintained HCV ribonucleic acid (RNA) less than (<) the lower limit of quantification (LLOQ) until LPVPS.

Arm type	other
Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received odalasvir as oral tablets in parent studies.

Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 as oral tablets in parent studies.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir as oral capsules in previous parent studies.

Arm title	No SVR at LPVPS

Arm description:

Subjects who completed the LPVPS (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of HCV infection, and who

agree to participate in this follow-up study was assessed for presence and long term-persistence of RAS and liver disease status.

Arm type	other
Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received odalasvir as oral tablets in parent studies.

Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 as oral tablets in parent studies.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received simeprevir as oral capsules in parent studies.

Number of subjects in period 1	SVR at LPVPS	No SVR at LPVPS
Started	53	1
Completed	53	0
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups

Reporting group title	SVR at LPVPS

Reporting group description:

Subjects who completed the last post-therapy visit of the parent study (LPVPS) (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of hepatitis C virus (HCV) infection, and who agreed to participate in this follow-up study was assessed for durability of sustained virologic response (SVR), incidence of late viral relapse, presence and long term-persistence of resistance associated substitutions (RAS) and liver disease status. SVR at the LPVPS is defined as subjects who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study, and maintained HCV ribonucleic acid (RNA) less than (<) the lower limit of quantification (LLOQ) until LPVPS.

Reporting group title	No SVR at LPVPS

Reporting group description:

Subjects who completed the LPVPS (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of HCV infection, and who agree to participate in this follow-up study was assessed for presence and long term-persistence of RAS and liver disease status.

Reporting group values	SVR at LPVPS	No SVR at LPVPS	Total
Number of subjects	53	1	54
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	51	1	52
From 65 to 84 years	2	0	2
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	57	51	
full range (min-max)	32 to 67	51 to 51	-
Title for Gender Units: subjects			
Female	21	0	21
Male	32	1	33

End points

End points reporting groups

Reporting group title	SVR at LPVPS

Reporting group description:

Subjects who completed the last post-therapy visit of the parent study (LPVPS) (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of hepatitis C virus (HCV) infection, and who agreed to participate in this follow-up study was assessed for durability of sustained virologic response (SVR), incidence of late viral relapse, presence and long term-persistence of resistance associated substitutions (RAS) and liver disease status. SVR at the LPVPS is defined as subjects who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study, and maintained HCV ribonucleic acid (RNA) less than (<) the lower limit of quantification (LLOQ) until LPVPS.

Reporting group title	No SVR at LPVPS

Reporting group description:

Subjects who completed the LPVPS (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of HCV infection, and who agree to participate in this follow-up study was assessed for presence and long term-persistence of RAS and liver disease status.

Subject analysis set title	SVR at LPVPS + No SVR at LPVPS
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects (SVR at LPVPS + No SVR at LPVPS) who received odalasvir and AL-335 with or without simeprevir in parent studies were followed up in this study. SVR at LPVPS is defined as subjects who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study and maintained HCV RNA < LLOQ until LPVPS.

Primary: Percentage of Subjects who Maintained Sustained Virologic Response (SVR) Until the End of the Long-Term Follow-up

End point title	Percentage of Subjects who Maintained Sustained Virologic Response (SVR) Until the End of the Long-Term Follow-up[1][2]

End point description:

Percentage of subjects who maintained SVR (if hepatitis C virus [HCV] ribonucleic acid [RNA] was less than [<] lower limit of quantification (LLOQ) (Detected or Not Detected) at each time point in the present study) was reported. Here 'endpoint' refers to the last available measurement in this study. Population included all enrolled subjects with SVR at last post therapy visit of the parent study (LPVPS). Here 'n' refers to number of subjects who were evaluable at each specified time point. If a measurement at a time point was missing but a measurement was available at a later time point, the missing measurement was imputed with the measurement at the later time point.

End point type	Primary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics (percentage and 95% confidence interval provided) were done, no inferential statistical analyses were performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	SVR at LPVPS			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Percentage of subjects				
number (confidence interval 95%)				

LPVPS (n=53)	100 (93.3 to 100)			
Month 6 (n=44)	100 (92.0 to 100)			
Month 12 (n=38)	100 (90.7 to 100)			
Month 18 (n=15)	100 (78.2 to 100)			
Endpoint (n=44)	100 (92.0 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Late Viral Relapse Among Subjects Who Achieved SVR at Last Post-therapy Visit of the Parent Study

End point title	Percentage of Subjects with Late Viral Relapse Among Subjects Who Achieved SVR at Last Post-therapy Visit of the Parent Study[3]

End point description:

Late viral relapse is defined as subjects who had achieved SVR at LPVPS but who had confirmed HCV RNA greater than or equal to (>=) LLOQ during follow-up in the present study. SVR at LPVPS is defined as subject who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study and maintained HCV RNA < LLOQ until LPVPS. Population included all enrolled subjects with SVR at LPVPS. Here 'n' refers to number of subjects who were evaluable at each specified time point. If a measurement at a time point is missing but a measurement is available at a later time window, the missing measurement is imputed with the measurement at the later time point.

End point type	Secondary

End point timeframe:

Months 6, 12 and 18 (up to 3 years)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	SVR at LPVPS			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Percentage of subjects				
number (confidence interval 95%)				
Month 6 (n=44)	0 (0 to 8.0)			
Month 12 (n=38)	0 (0 to 9.3)			
Month 18 (n=15)	0 (0 to 21.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Albumin Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Albumin Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in albumin levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an informed consent form (ICF) for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: grams per liter (g/L)				
arithmetic mean (standard deviation)				
LPVPS (n=54)	38.5 (± 4.66)			
Month 6 (n=27)	6.4 (± 3.89)			
Month 12 (n=38)	8.0 (± 2.47)			
Month 18 (n=15)	8.5 (± 2.80)			
Endpoint (n=46)	7.4 (± 3.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Alanine Aminotransferase Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Alanine Aminotransferase Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in alanine aminotransferase levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: Units per liter (U/L)				
arithmetic mean (standard deviation)				
LPVPS (n=54)	19.1 (± 8.89)			
Month 6 (n=27)	-1.8 (± 7.67)			
Month 12 (n=38)	-0.3 (± 8.11)			
Month 18 (n=15)	-2.1 (± 8.22)			
Endpoint (n=46)	-0.9 (± 8.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Alkaline Phosphatase Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Alkaline Phosphatase Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in alkaline phosphatase levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: U/L				
arithmetic mean (standard deviation)				
LPVPS (n=54)	65.2 (± 20.86)			
Month 6 (n=27)	2.5 (± 13.42)			
Month 12 (n=38)	4.9 (± 12.51)			
Month 18 (n=15)	4.1 (± 9.51)			
Endpoint (n=46)	4.6 (± 12.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Aspartate Aminotransferase Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Aspartate Aminotransferase Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in aspartate aminotransferase levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: U/L				
arithmetic mean (standard deviation)				
LPVPS (n=54)	22.3 (± 7.00)			
Month 6 (n=27)	-2.2 (± 4.08)			
Month 12 (n=38)	-0.7 (± 6.11)			
Month 18 (n=15)	-3.3 (± 8.11)			
Endpoint (n=46)	-1.9 (± 6.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Bilirubin Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Bilirubin Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in bilirubin levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: micromole per liter (umol/L)				
arithmetic mean (standard deviation)				
LPVPS (n=54)	10.0 (± 7.11)			
Month 6 (n=27)	-1.5 (± 3.84)			
Month 12 (n=38)	-1.6 (± 4.73)			
Month 18 (n=15)	-1.0 (± 3.12)			
Endpoint (n=46)	-1.2 (± 3.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Direct Bilirubin Levels at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Direct Bilirubin Levels at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in direct bilirubin levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: umol/L				
arithmetic mean (standard deviation)				
LPVPS (n=54)	4.0 (± 1.73)			
Month 6 (n=27)	-2.3 (± 1.11)			
Month 12 (n=38)	-2.6 (± 1.05)			
Month 18 (n=15)	-2.7 (± 1.03)			
Endpoint (n=46)	-2.4 (± 1.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Indirect Bilirubin Levels at Month 6 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Indirect Bilirubin Levels at Month 6 and Endpoint

End point description:

Change from LPVPS in indirect bilirubin levels to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Month 6 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: umol/L				
arithmetic mean (standard deviation)				
LPVPS (n=11)	7.6 (± 4.25)			
Month 6 (n=3)	-2.3 (± 2.08)			
Endpoint (n=3)	-2.3 (± 2.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Activated Partial Thromboplastin Time (aPTT) at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Activated Partial Thromboplastin Time (aPTT) at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in aPTT to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: seconds (s)				
median (full range (min-max))				
LPVPS (n=54)	31.00 (22.6 to 37.0)			
Month 6 (n=27)	-6.00 (-9.6 to 1.2)			
Month 12 (n=35)	-6.20 (-12.3 to 7.6)			
Month 18 (n=15)	-7.20 (-8.9 to -2.9)			
Endpoint (n=46)	-6.35 (-12.3 to 7.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Prothrombin International Normalized Ratio (INR) at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Prothrombin International Normalized Ratio (INR) at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in prothrombin INR to the last available measurement was reported as measure (endpoint) of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: Ratio				
arithmetic mean (standard deviation)				
LPVPS (n=54)	1.00 (± 0.073)			
Month 6 (n=27)	-0.05 (± 0.070)			
Month 12 (n=35)	-0.05 (± 0.066)			
Month 18 (n=15)	-0.03 (± 0.070)			
Endpoint (n=46)	-0.03 (± 0.059)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Last Post-therapy Visit of the Parent Study in Prothrombin Time at Month 6, 12, 18 and Endpoint

End point title	Change from Last Post-therapy Visit of the Parent Study in Prothrombin Time at Month 6, 12, 18 and Endpoint

End point description:

Change from LPVPS in prothrombin time to the last available measurement (endpoint) was reported as measure of liver disease status. All enrolled analysis set included all subjects who signed an ICF for the present study. Here 'n' refers to number of subjects who were evaluable at each time point.

End point type	Secondary

End point timeframe:

LPVPS, Months 6, 12, 18 and Endpoint (up to 3 years)

End point values	SVR at LPVPS + No SVR at LPVPS			
Subject group type	Subject analysis set			
Number of subjects analysed	54			
Units: seconds				
median (full range (min-max))				
LPVPS (n=54) Month 6 (n=27) Month 12 (n=35) Month 18 (n=15) Endpoint (n=46)	13.35 (9.7 to 17.0) -3.10 (-5.8 to 0.2) -3.50 (-5.8 to -2.6) -3.70 (-5.8 to -2.6) -3.40 (-5.8 to 0.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Each Child-Pugh Grading Category at Endpoint

End point title	Number of Subjects in Each Child-Pugh Grading Category at Endpoint

End point description:

Number of subjects in each child-pugh grading category at endpoint was reported. The five clinical measures of liver disease, subsequently used to derive the Child-Pugh score are as followed :1-

Encephalopathy grade, 2- Ascites, 3- Serum bilirubin milligram per deciliter (mg/dL), 4-Serum albumin gram per liter (g/L), 5- Prothrombin time, seconds prolonged. Each measure is scored from 1 to 3, with 3 indicating most severe derangement. In subjects with cirrhosis, the sum of the scores provides the child-pugh score as followed: child-pugh A (mild): 5-6 points, child-pugh B (moderate): 7-9 points, and child-pugh C (severe): 10-15 points. All enrolled analysis set included all subjects who signed an ICF for the present study with cirrhosis at baseline.

End point type	Secondary

End point timeframe:

LPVPS to Endpoint (up to 3 years)

End point values	SVR at LPVPS	No SVR at LPVPS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	0[4]		
Units: Subjects				
Mild	2			
Moderate	0			
Severe	0			

Notes:

[4] - No subjects with child-pugh liver disease grading + cirrhosis at baseline and without SVR at LPVPS.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Each Liver Ultrasound Interpretation Result Category at Endpoint

End point title	Number of Subjects in Each Liver Ultrasound Interpretation Result Category at Endpoint

End point description:

The number of subjects in each liver ultrasound interpretation result category (normal or abnormal) at endpoint is reported. All enrolled analysis set included all subjects who signed an ICF for the present study with cirrhosis at baseline in 'SVR at LPVPS' group and subjects with metavir score F3 or F4 for 'No SVR at LPVPS' group. Here 'endpoint' refers to the last available measurement in this study.

End point type	Secondary

End point timeframe:

LPVPS to Endpoint (up to 3 years)

End point values	SVR at LPVPS	No SVR at LPVPS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: Subjects				
Abnormal	0	0		
Normal	2	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years

Adverse event reporting additional description:

Safety analysis set included all subjects who received at least 1 dose of study treatment in a previous Phase 2 study and were enrolled into the present study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	No SVR at LPVPS

Reporting group description:

Subjects who completed the LPVPS (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of HCV infection, and who agree to participate in this follow-up study was assessed for presence and long term-persistence of RAS and liver disease status. SVR at LPVPS is defined as subjects who achieved SVR12 in the parent study and maintained HCV RNA < LLOQ until LPVPS.

Reporting group title	SVR at LPVPS

Reporting group description:

Subjects who completed the last post-therapy visit of the parent study (LPVPS) (Phase 2 or Phase 3 study), in which they received a regimen containing odalasvir and AL-335 with or without simeprevir for the treatment of hepatitis C virus (HCV) infection, and who agreed to participate in this follow-up study was assessed for durability of sustained virologic response (SVR), incidence of late viral relapse, presence and long term-persistence of resistance associated substitutions (RAS) and liver disease status. SVR at the LPVPS is defined as subjects who achieved SVR 12 weeks after the end of treatment (SVR12) in the parent study, and maintained HCV ribonucleic acid (RNA) less than (<) the lower limit of quantification (LLOQ) until LPVPS.

Serious adverse events	No SVR at LPVPS	SVR at LPVPS	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 53 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	No SVR at LPVPS	SVR at LPVPS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 53 (1.89%)	
Cardiac disorders			

Supraventricular Tachycardia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 53 (1.89%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2017	The overall reason for the amendment was the decision to discontinue further development of JNJ-64294178 (a combination of three direct acting antivirals - AL-335, odalasvir , and simeprevir), and consequently, the stop of further enrollment in the current study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the early termination of study, only 54 of planned 250 subjects were enrolled, and no subjects completed full 36-month follow-up period. Consequently, only limited long-term follow-up data was available and conclusions could not be drawn.

Notes: